PATENT
ATTORNEY DOCKET NO: 582.02

REMARKS

This paper is being filed in response to an Office Action dated October 3, 2003. Upon entry of the amendments presented herein, claims 1, 3-6 and 8-13 remaining pending in the present application. Claims 2 and 7 have been canceled by this amendment, and claims 1 and 10 have been amended.

Claim 1 has been amended to recite a method of treating "discogenic pain, intradiscal administration of a vanilloid receptor 1 agonist in an amount sufficient to ablate neurons." Since support for this amendment can be found in the originally filed claims and in the specification, *inter alia*, canceled claim 2 and p. 10, lines 16 and 17, applicant submit that no new matter has been added by this amendment to claim 1.

Claim 10 has been amended to recite that the kit has compartment containing a vanilloid receptor agonist in an amount sufficient to relieve "discogenic pain" and that the instructional material includes "instructions for intradiscal administration of the vanilloid receptor 1 agonist." Since this amendment is supported by the originally filed claims and the specification, applicant submits that no new matter has been added by this amendment to claim 10.

Section 112 Rejection

Claims 1-9 have been rejected under 35 U.S.C. § 112, first paragraph. The examiner asserts that the specification does not reasonably provide enablement for methods of treating any type of pain by administering any Vanilloid Receptor 1 ("VR1") agonist. When viewed in light of the seven factors described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), the examiner asserts that one skilled in the art could not practice the invention without undue experimentation. Applicant respectfully traverses this rejection in view of the amendments presented herein.

Applicant has amended claim 1 to recite a method of treating "discogenic pain." In view of this amendment, applicant respectfully submits that the originally filed specification provides sufficient enablement for the inventions of claims 1 and 3-9 directed to a method of treating discogenic pain. The term VR1 agonist is defined at p. 4, lines 1-3 as a compound that binds to VR1 and stimulates calcium uptake. Suitable vanilloid receptor agonists are described in the specification, *inter alia*, from p. 6, line 14 to p. 8, line 10, which include capsaicin and its analogs. In addition, other suitable VR1 agonists can be identified by the skilled artisan without undue experimentation by utilizing well-known methodologies described in the specification,

inter alia, from p. 8, line 12 to p. 10, line 3. Applicant, therefore, respectfully requests withdrawal of this rejection.

Section 102 Rejections

Claim 1, 3, 5, and 6 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Szabo et al., Brain Research 840, 02-98 (1999) ("Szabo"). Referencing the abstract and pp. 92-93 of Szabo, the examiner relies on Szabo's alleged disclosure of methods for providing prolonged regional analgesia for pain in rats comprising injecting RTX, a VR1 agonist, directly and intrathecally through an epidural catheter. Applicant respectfully traverses this rejection in view of the amendments presented herein.

Applicant has amended claim 1 to require "intradiscal administration of a vanilloid receptor 1 agonist." Szabo, however, fails to teach or suggest the intradiscal administration of a VR1 agonist. Applicant, therefore, respectfully requests withdrawal of this rejection because Szabo fails to teach each and every element of independent claim 1 and claims 3, 5, and 6, which all depend from claim 1.

Claims 1, 3-6, and 8-13 have been rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Iadarola et al., WO 02/076444 ("Iadarola"). Referencing pp. 13, 14, and 21-23 of Iadarola, the examiner relies on Iadarola's alleged disclosure of a rat animal mode for treating chronic pain by ablating VR1 agonist sensitive neurons, which includes administering capsaicin and RTX intrathecally or intraganglionically. The examiner also asserts that Iadarola further discloses the use of a local anesthetic, such as lidocaine and bupivacaine in combination with capsaicin (pp. 15 and 16), and pharmaceutical kits, which include a VR1 agonist, a local anesthetic and instruction material (pp. 16 and 20).

Claim 1 has been amended to require "intradiscal administration of a vanilloid receptor 1 agonist" to treat "discogenic pain," and claim 10 has been amended to recite "an amount sufficient to relieve discogenic pain" and "instructions for intradiscal administration of the vanilloid receptor 1 agonist." As recognized by the examiner at p. 7 of the office action, Iadarola fails to teach or suggest the intradiscal administration of a VR1 agonist for treatment of discogenic pain. Applicant, therefore, respectfully requests withdrawal of this rejection because Iadarola fails to teach each and every element of independent claims 1 and 10. Withdrawal of this rejection for dependent claims 3-6, 8, and 9 (which depend from claim 1) and dependent

claim 11-13 (which depend directly or indirectly from claim 10) is also respectfully requested for the same reasons discussed above.

Section 103 Rejection

Claims 1-13 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Iadarola in view of Takahashi et al., Neuroscience Letters, 161, 1-3 (1999) ("Takahashi"). The examiner relies on Iadarola for allegedly disclosing the use of VR1 agonists to ablate C-fiber neurons and the use of his methods for treating pain affecting the spinal column, but acknowledges the failure of Iadarola to teach or suggest treatment of discogenic pain or administration of a VR1 agonist by direct injection into the space between vertebrae. Referencing p. 1, ¶¶ 2 and 4, p. 2, ¶2 of Takahashi, the examiner relies on Takahashi for allegedly disclosing direct administration of capsaicin, a VR1 agonist, into the "annulus fibrosus of a disc in a rat using a microsyringe "for pain that are caused by lesions in spinal disc." The examiner also references Takahashi's further suggestion in the abstract and at p. 3, last paragraph, regarding the presence of sensory C-fibers that innervate the intervertebral discs and their potential role in treating pain associated with disc lesions.

The examiner then opines that the skilled artisan would have modified Iadarola's methodology to directly administer VR1 agonist into the space between vertebrae including annulus fibrosus to treat discogenic pain of the spinal column. The examiner further asserts that the skilled artisan would have been motivated to undergo such a modification, because (i) Takahashi teaches that lesions within the spinal discs are innervated by c-fibers and (ii) one of ordinary skill in the art would have had a reasonable expectation of success in providing the pharmacological effects of VR1 agonists when administering them in the vertebral space. Applicant respectfully traverses this rejection.

As recognized by the examiner, Iadarola fails to teach or suggest treatment of discogenic pain by intradiscal administration of a VR1 agonist. For example, at page 4, Iadarola lists a large number of pain types, but does not mention discogenic pain, which is believed to be generated locally by C fiber endings in the disc. Rather, Iadarola describes VR1 injections into sensory ganglia, which is a treatment intended to affect pain over a relatively wide (segmental) area, distant from the site of the injection. Treatment of ganglia ablates sensory cell bodies, as opposed to endings, and alters pain at sites that may be a meter or more away from the injection

site. In contrast, the present invention requires intradiscal treatment, which ablates sensory endings and decreases pain generation at the site of injection.

Applicant respectfully submits that Takahashi is similarly deficient. Takahashi's work is primarily intended to give evidence of a potential mechanism for referred groin pain that can occur with disc injury. Thus, Takahashi injected VR1 agonist into the annulus fibrosus to determine if there was a direct connection between discal afferents and groin afferents. There was no mention or suggestion in Takahashi's paper of intradiscal injections as a treatment of discogenic back pain. In fact, capsaicin was used to determine dye extravasation in the groin skin, not treatment of discogentic pain. (*See* abstract, Experiments 1 and 2 on p. 324, and results on p. 325.) Accordingly, applicant respectfully submits that the examiner is improperly using hindsight to equate the suggestion of the presence of afferent C fibers in Takahashi to the problem recognized by the presently claimed invention. Because of these distinctions, applicant respectfully submits that it would not have been obvious for the skilled artisan to combine Iadarola's ganglionic injections for killing sensory nerve cell bodies to control pain with Takahashi's mechanistic studies of discal nerve branching to obtain the originally filed claims or the presently amended claims. Applicant, therefore, respectfully requests withdrawal of this Section 103 rejection.

Conclusion

Applicants believe they have provided a complete response to the outstanding office action. For the reasons articulated above, reconsideration and allowance of this patent application is respectfully requested.

Respectfully submitted,
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